were prepared in a eukaryotic expression vector and expressed in cultured cells by transient transfection, in the presence or absence of actinomycin D.
Results: No mutations were identified in the *transthyretin* gene. A C to T substitution of nucleotide 635 of *desmin*, resulting in the replacement of alanine 212 by valine (A212V) was identified in one family with isolated RCM. Expression of the wild type and mutant proteins in cultured myocytes showed no difference in the desmin filamentous network. However, exposure of these cells to actinomycin D resulted in increased filament disarray and cell death in cells expressing A212V desmin.
Conclusions: Here we describe a novel mutation in the *desmin* gene in a family with RCM. The increased susceptibility of myocytes expressing this mutation to actinomycin-induced cell death suggest a possible role of apoptosis in the pathologic events leading to RCM.

ORAL CONTRIBUTIONS

827 Modeling Outcomes and Cost

Monday, March 18, 2002, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 255W

2:00 p.m.

827-1 Does the Evidence Support the Verdict of High Profile Clinical Trials? A Conventional Versus Bayesian Perspective

Sanjay Kaul, Matthew J. Price, Sriram Padmanabhan, Vladimir Rukshin, George A. Diamond, *Cedars Sinai Medical Center, Los Angeles, California, UCLA School of Medicine, Los Angeles, California.*

Background: Conventional significance tests frequently characterize clinically negligible differences as being 'statistically significant'. **Objective:** To perform a Bayesian analysis of clinical trials and compare it with the conventional two-sided p value. **Methods:** Seven high profile trials (those having a major impact on CAD treatment) reported in the last 5 years were identified for analysis. Results are expressed in odds ratio (OR) and associated 95% confidence interval (CI), two-sided p value (using a chi square test), number needed to treat (NNT) to avoid 1 event (the inverse of the absolute risk reduction), probability of benefit (pb) based on Bayesian analysis, and adjusted NNT (NNT/pb). **Results:** The results of the 2 analyses were discordant ($p<0.05$ and $p_b<95\%$) in 5 and concordant ($p<0.05$ and $p_b>95\%$) in 2 out of 7 trials. The probability of benefit in the discordant trials was low ranging from 7% for clopidogrel in CAPRIE to 30% for carvedilol in CAPRICORN despite statistically significant odds ratios and p values. The corresponding adjusted NNT values increased from a range of 29-115 to 94-3833. **Conclusions:** The conventional p value threshold is too liberal and does not correspond with Bayesian threshold of >95% probability. Investigators should rely on Bayesian analyses to safeguard against such errors leading to inappropriate claims. Alternatively, a more stringent conventional p value threshold, e.g., <0.01 to <0.001 should be chosen.

Trial	N	Endpoint	OR (95% CI)	p value	NNT	pb	Adjusted NNT
CAPRIE (Clopidogrel in Vascular disease)	19413	Death, MI or stroke @ 1-3y	0.91 (0.83,1.00)	0.047	115	0.07	3833
EPISTENT (Abciximab in Coronary Stenting)	1603	Death @ 1y	0.42 (0.18,0.97)	0.037	75	0.12	625
ESSENCE + TIMI-11B (Enoxaparin in Acute Coronary Syndrome	7081	Death or MI @ 14d	0.79 (0.69,0.90)	0.016	75	0.20	375
MIRACL (Atorvastatin in Acute Coronary Syndrome)	3086	Death, MI or ischemia @ 4m	0.83 (0.68,1.00)	0.048	39	0.18	218
CAPRICORN (Carvedilol in Post-MI LV Dysfunction)	1959	Death @ 1.3y	0.74 (0.57,0.97)	0.026	29	0.31	94
HOPE (Ramipril in Seconary Prevention of CVD)	9297	Death, MI or stroke @ 5y	0.75 (0.68,0.84)	<0.001	27	>0.99	27
Lyon Diet Heart Study (Mediterranean Diet for Secondary Prevention)	423	Death or MI @ 46m	0.25 (0.13,0.47)	<0.001	7	>0.99	7

2:15 p.m.

827-2 Do Glycoprotein 2B3A Inhibitors Reduce Mortality? A Bayesian Meta-Analysis

Sanjay Kaul, Matthew J. Price, Sriram Padmanabhan, Vladimir Rukshin, George A. Diamond, *Cedars Sinai Medical Center, Los Angeles, California, UCLA School of Medicine, Los Angeles, California.*

Background: Although nearly 50000 patients have been enrolled in clinical trials of glycoprotein 2b3a inhibitors (GPIs), the issue of their effect on cardiac mortality remains controversial, in part, because conventional tests of statistical significance are unreliable when applied to such large samples. **Objective:** To perform a Bayesian meta-analysis of the effect of GPIs on total mortality, and compare the resultant probability of benefit with the conventional p value. **Methods:** A total of 20 randomized trials involving 48584 patients were identified for analysis at 30 d and 5 trials involving 10959 patients for analysis at 1 year. Pooled trial results are expressed in terms of the odds ratio (OR) and associated 95% confidence interval (CI), the two-sided p value (using a chi square test), the probability of benefit (p_b) based on Bayesian analysis, and number needed to treat (NNT) to avoid 1 mortality (the inverse of the absolute risk reduction). **Results:** At 30 days, there were 672 deaths among 27073 GPI and 590 deaths among 21511 placebo patients [OR = 0.90 (0.81, 1.01), p = 0.08, p_b = 0.02, NNT = 384]. At 1 year, there were 251 deaths among 6729 GPI and 183 deaths among 4230 placebo patients [OR = 0.86 (0.71, 1.04), p = 0.12, p_b = 0.03, NNT = 168]. Thus, the probability that GPI therapy reduced total mortality was very low (2% at 30 days and 3% at 1 year) despite odds ratios and p values that tended toward statistical significance. Four trials of abciximab were analyzed separately (EPIC, EPILOG, EPISTENT, CADILLAC). At 1 year, there were 127 deaths among 5205 abciximab and 118 deaths among 3472 placebo patients [OR = 0.72 (0.56, 0.93), p = 0.01, p_b = 0.19, NNT = 108]. The best conventional estimate was a 0.93% absolute reduction in mortality with abciximab among 8677 patients. However, there was only a 19% probability that abciximab was superior to placebo despite conventional statistical significance. **Conclusion:** The widespread belief that GPIs, specifically abciximab, confer a significant mortality benefit is directly controverted by this Bayesian meta-analysis. Future large-scale clinical trials should incorporate the Bayesian approach in their design and analysis in order to minimize the potential for such errors.

2:30 p.m.

827-3 Cost-Effectiveness of Prophylactic Amiodarone Therapy for the Prevention of Atrial Fibrillation in Patients Undergoing Cardiac Surgery Varies by Underlying Risk and Type of Surgery: Results for CABG, Valve Replacement, and Combined CABG and Valve Replacement

Elizabeth M. Mahoney, Jovonne K. Williams, Emir Veledar, Trevor D. Thompson, William S. Weintraub, *Emory University School of Medicine, Atlanta, Georgia.*

Background. The selection of patients (pts) for whom prophylactic amiodarone therapy to prevent atrial fibrillation (AF) following cardiac surgery is cost-effective (CE) is difficult. This study adds to previous efforts by separately examining the risk and added costs of AF in CABG, valve replacement (VR) and combined CABG and VR (CABG+VR) pts.
Methods. Outcomes and costs for 8709 CABG, 1217 VR and 624 CABG+VR pts at Emory University Hospitals from 1/94-6/99 were used to examine the CE of targeted amiodarone therapy for each of the three types of surgical patients. Logistic regression was used to develop models for the prediction of AF and linear regression was used to predict hospital costs, including the additional costs attributed to AF. Predicted probabilities from the logistic models were used as the index from which to identify patient subsets to be targeted for therapy. Marginal CE of targeting therapy to subsets at incrementally lower levels of risk was evaluated. CE was evaluated as cost/episode of AF averted. Effectiveness of amiodarone was assumed to be 26% (ARCH trial) and cost $973 (7 amps/day for 2 days at $69.50/amp).
Results. AF rates were 17.7% for CABG, 24.6% for VR and 33.8% for CABG+VR.

Treatment Threshold: Probability of AF	CABG: % treated	CABG: marginal cost/AF averted	VR: % treated	VR: marginal cost/AF averted	CABG+VR: % treated	CABG+VR: marginal cost/AF averted
0	100	$55,854	100	$43,011	100	$39,698
10	77.7	$34,087	91.7	$27,061	99.0	$22,009
15	55.5	$25,224	78.0	$18,658	95.4	$14,325
20	36.4	$20,540	60.6	$13,687	88.6	$9,903
25	21.3	$17,479	44.6	$10,603	76.0	$7,178
30	10.6	$15,406	32.2	$8,626	63.8	$4,947
35	4.2	$13,864	19.1	$7,179	42.6	$3,430
40	1.5	$12,696	9.1	$5,990	27.9	$2,346
45	0.5	$11,789	3.5	$5,089	14.4	$1,423
50	0.1	--	1.1	--	9.3	--

Conclusions: Using $5000 as an acceptable cost/AF averted, prophylactic amiodarone use in CABG pts is not cost-effective. Therapy would be recommended for a small fraction of VR pts who have a predicted risk of AF>45% and roughly 2/3 of CABG+VR pts who have a predicted risk of AF>30%. Nomograms can help identify these pts.

2:45 p.m.

827-4 The Intermountain Risk Model: Predicting Mortality by Traditional and Novel Risk Factors Among Patients With Significant Coronary Disease

Benjamin D. Horne, Joseph B. Muhlestein, Chloe A. Allen Maycock, John F. Carlquist, Donald L. Lappe', Robert R. Pearson, Dale G. Renlund, Jeffrey L. Anderson, *LDS Hospital, Salt Lake City, Utah, University of Utah, Salt Lake City, Utah.*

Background: Although treatment guidelines exist for guiding the therapy of patients with diagnosed coronary artery disease (CAD), they are largely based on risk models that predict CAD onset, not mortality after disease has developed. No mortality risk model has been created with data from the general CAD patient population. This study evaluated predictive risk models for mortality among patients with significant, angiographically-defined CAD.
Methods: The catheterization registry of the Intermountain Heart Collaborative Study provided a cohort of 2,585 patients with significant, angiographically-proven CAD (≥1 lesion of ≥70% stenosis). At angiography, 15 traditional and 3 novel (C-reactive protein [CRP], cytomegalovirus [CMV], homocysteine [HCY]) risk factors were measured. Patients were followed for 2.4±1.6 years (maximum: 5.8 years) to determine the incidence of mortality.
Results: Average age was 65±11 years, 76% were male, and 250 (9.7%) died. Predic-